APPENDIX A

PATENT
Attorney Docket No. **MSU-08604**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

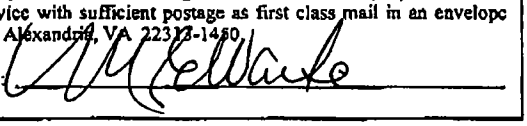
In re Application of: Dean DellaPenna *et al.*
Serial No.: 10/751,235 Group No.: 1638
Filed: 01/02/2004 Examiner: Worley, C.K.
Entitled: **Novel Carotenoid Hydroxylases For Use In Engineering Carotenoid Metabolism In Plants**

DECLARATION OF DR. DEAN DELLAPENNA PURSUANT TO 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: May 18, 2007 By: 

I, Dr. Dean DellaPenna, state that:

1. I am a joint inventor of the subject matter claimed in the above captioned United States Patent Application. I am a Professor in the Department of Biochemistry and Molecular Biology at Michigan State University.

2. It is my understanding that the examiner has rejected claims to vectors and the use of nucleic acid sequences encoding proteins with greater than 80% identity to LUT1 (i.e., SEQ ID NO:4). In particular, the Examiner has alleged that the specification does not describe any structural features that correspond to the functional activity of being able to complement the *lut1* mutation and does not provide support for the genus of nucleic acid sequences encoding proteins that are at least 80% identical to SEQ ID NO:4.

I do not agree with the Examiner's allegations. One example of "one of skill in the art" in the field of plant genetics and molecular biology is a person with about 2 to 4 years of post-doctoral research experience. My experience exceeds this example. The specification provides the structure for SEQ ID NO:4 and homologs such as rice CYP97C (LUT1; SEQ ID NO:16). The person of skill in the art would be able to make or identify nucleic acid sequences encoding proteins that are at least 72% identical to SEQ ID NO:4 (Figure 9). Many methods for making sequences with the requisite identity are taught in the specification, for example, at pages 51-64. The specification further teaches methods for screening for functional LUT1 sequences by complementation of LUT1 mutants in Examples 3 and 5. This structural information and the screening procedures allows the person of skill in the art to identify a genus of nucleic acid sequences encoding proteins at least 72% identical to SEQ ID NO:4 that have functional LUT1 activity as claimed.

3. It is also my understanding that the Examiner's position is that one of skill in the art would not know how to use the claimed nucleic acids and vectors for prokaryotic or yeast expression. This is not a scientifically valid argument. A person of ordinary skill in the art, as defined above, would be able to express the claimed sequences in bacteria or yeast using the methods taught in the present application or otherwise known in the art. For example, Quinlan *et al.*, used Escherichia coli as a platform for functional expression of plant P450 carotene hydroxylases, Archives of Biochemistry and Biophysics 458 (2007) 146–157, have recently described the transfection of a prokaryotic expression vector comprising a CYP97C (LUT1) nucleic acid coding sequence into bacteria for expressing a plant ε-ring hydroxylase. Specifically, Quinlan *et al.*, used an Arabidopsis CYP97C (LUT1) of the present invention (SEQ ID NO:04) coding sequence to obtain a Oryza sativa (rice) LUT1 homolog (GenBank #AK065689). As stated in the patent, the Arabidopsis gene sequence (SEQ ID NO:05) was used by a person of ordinary skill in the art to identify this related rice gene. This paper further demonstrated that expression of the rice LUT1 homolog resulted in a change in carotenoid production from the bacteria expressing rice LUT1 relative to both bacteria transformed with a β-hydroxylase coding sequence and bacteria transformed with a control vector. In

particular, bacteria that expressed plant ε-ring hydroxylase showed a loss of a lutein precursor lycopene (φ, φ -carotene) associated with a gain of ε, φ - carotene product (δ-carotene) and ε, ε -carotene product (lactucaxanthin). Furthermore the Oryza sativa (rice) LUT1 homolog (GenBank #AK065689) nucleic acid homolog (SEQ ID NO:22 and amino acid sequence SEQ ID NO:16) was disclosed in the present application. Moreover, Arabidopsis LUT1 (SEQ ID NO:04) disclosed in the present inventions was described in the instant application as showing 78% amino acid sequence homology to Oryza sativa (rice) LUT1 amino acid homolog encoded by a nucleic acid sequence located at GenBank #AK065689 (SEQ ID NO:16) (Figures 9 and 23). This shows that sequences with the requisite identity function as claimed and that persons of ordinary skill in the art would be able to use the sequences as claimed.

4. I further declare that all statement made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: May 18, 2007

Dr. Dean DellaPenna